10 20 30 40 50 60 70 CACGGATCGG GAGATCTCCC GATCCCCTAT GGTCGACTCT CAGTACAATC TGCTCTGATG CCGCATAGTT 80 90 100 110 120 130 140 AAGCCAGTAT CTGCTCCCTG CTTGTGTGTT GGAGGTCGCT GAGTAGTGCG CGAGCAAAAT TTAAGCTACA 150 160 170 180 190 200 210 ACAAGGCAAG GCTTGACCGA CAATTGCATG AAGAATCTGC TTAGGGTTAG GCGTTTTGCG CTGCTTCGCG 220 230 240 250 260 270 280 ATGTACGGGC CAGATATACG CGTTGACATT GATTATTGAC TAGTTATTAA TAGTAATCAA TTACGGGGTC 290 300 310 320 330 340 350 ATTAGTTCAT AGCCCATATA TGGAGTTCCG CGTTACATAA CTTACGGTAA ATGGCCCGCC TGGCTGACCG ... 360 370 380 390 400 410 CCCAACGACC CCCGCCCATT GACGTCAATA ATGACGTATG TTCCCATAGT AACGCCAATA GGGACTTTCC 430 440 450 460 470 480 490 ATTGACGTCA ATGGGTGGAC TATTTACGGT AAACTGCCCA CTTGGCAGTA CATCAAGTGT ATCATATGCC 500 510 520 530 540 550 560 AAGTACGCCC CCTATTGACG TCAATGACGG TAAATGGCCC GCCTGGCATT ATGCCCAGTA CATGACCTTA 570 580 590 600 610 620 630 TOGGRACITIC CTACTTGGCA GTACATCIAC GTATTAGTCA TCGCTATTAC CATGGTGATG CGGTTTTGGC 640 650 660 670 680 690 700 AGTACATCAN TGGGCGTGGA TAGCGGTTTG ACTCACGGGG ATTTCCAAGT CTCCACCCCA TTGACGTCAA 710 720 730 740 750 760 770 TGGGAGTTTG TTTTGGCACC AAAATCAACG GGACTTTCCA AAATGTCGTA ACAACTCCGC CCCATTGACG 780 790 800 810 820 830 CARATGGGCG GTAGGCGTGT ACGGTGGGAG GTCTATATAA GCAGAGCTCT CTGGCTAACT AGAGAACCCA CTGCTTARCT GGCTTATCGA AATTAATACG ACTCACTATA GGGAGACCCA AGCTTCGCAG AATTCCTGCG 920 930 940 950 960 970 980 GCTGCTACAG TGTGTCCAGC GTCCTGCCTG GCTGTGCTGA GUGCTGGAAC AGTGGCGCAT CATTCAAGTG 990 1000 1010 1020 1030 1040 1050 CACAGTTACC CATCCTGAGT CTGGCACCTT AACTGGCACA ATTGCCAAAG TCACAGGTGA GCTCAGATGC

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 AAC TTC ACC CAC CTG GAC GGG TAC CTG GAC CTT CTC AGG GAG AAC CAG CTC CTC CCA
 Asn Phe Thr His Leu Asp Gly Tyr Leu Asp Leu Leu Arg Glu Asn Gln Leu Leu Pro>
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                           1970
 GGG TTT GAG CTG ATG GGC AGC GCC TCG GGC CAC TTC ACT GAC TTT GAG GAC AAG CAG
 Gly Phe Glu Leu Met Gly Ser Ala Ser Gly His Phe Thr Asp Phe Glu Asp Lys Gln>
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 CAG GTG TTT GAG TGG AAG GAC TTG GTC TCC AGC CTG GCC AGG AGA TAC ATC GGT AGG
 Gin Val Phe Glu Trp Lys Asp Leu Val Ser Ser Leu Ala Arg Arg Tyr Ile Gly Arg>
 a_a_a_a_a_a_a_ORF RF(1)_a_a_a_a_a_a_a_a_>
              2070 2080 2090 2100
 TAC GGA CTG GCG CAT GTT TCC AAG TGG AAC TTC GAG ACG TGG AAT GAG CCA-GAC CAC
 Tyr Gly Leu Ala His Val Ser Lys Trp Asn Phe Glu Thr Trp Asn Glu Pro Asp His>
 a a a a a a a ORF RF(1) a a a a a a a a a
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 CAC GAC TIT GAC AAC GTC TCC ATG ACC ATG CAA GGC TTC CTG AAC TAC TAC GAT! GCC
 His Asp Phe Asp Asn Val Ser Met Thr Met Gln Gly Phe Leu Asn Tyr Tyr Asp Ala>
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                  2190
 TGC TCG GAG GGT CTG CGC GCC GCC AGC CCC GCC CTG CGG CTG GGA GGC CCC GGC GAC
 Cys Ser Glu Gly Leu Arg Ala Ala Ser Pro Ala Leu Arg Leu Gly Gly Pro Gly Asp>
    a a a a a a CRF RF[1] a a a a a a a a a
                                            2270
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  TCC TTC CAC ACC CCA CCG CGA TCC CCG CTG AGC TGG GGC CTC CTG CGC CAC TGC CAC
  Ser Phe Eis Thr Pro Pro Arg Ser Pro Leu Ser Trp Gly Leu Leu Arg Eis Cys Eis>
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  GAC GGT ACC AAC TTC TTC ACT GGG GAG GCG GGC GTG CGG CTG GAC TAC ATC TCC CTC
  Asp Gly Thr Asn Phe Phe Thr Gly Glu Ala Gly Val Arg Leu Asp Tyr Ile Ser Leu>
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                  2360
                              2370
  CAC AGG AAG GGT GCG CGC AGC TCC ATC TCC ATC CTG GAG CAG GAG AAG GTC GTC GCG
  His Arg Lys Gly Ala Arg Ser Ser Ile Ser Ile Leu Glu Gln Glu Lys Val Val Ala>
  a a a a a a a ORF RF(1) a a a a a a a a
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  CAG CAG ATC CGG CAG CTC TTC CCC AAG TTC GCG GAC ACC CCC ATT TAC AAC GAC GAG
  Gln Gln Ile Arg Gln Leu Phe Pro Lys Phe Ala Asp Thr Pro Ile Tyr Asn Asp Glu>
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27	* CTG		GAT	* GAG		* CAG											GTC Val		
27	* CTG	Leu	GAT Asp	GAG Glu	Glu	* CAG Gln	Leu		Ala	Glu	Val	Ser	Gla	Ala	Gly	Thr	Val	Leu	
27	t CTG Leu	Leu a	GAT Asp	GAG Glu	Glu L	* CAG Gln	Leu	Trp	Ala	Glu	Val	Ser a	Gla	Ala a	Gly a	Thr	Val aa	Leu La	
27	CTG Leu	Leu a; 00 *	GAT qek s	GAG Glu aa	Glu a; BlO	CAG Gln a	Leu a;	Trp a 2820	Ala CRF	Glu RF[Val 1]	Ser 2 30 *	Gln a	Ala a2	Gly a 840	Thr a	Val aa	Leu 2950	<>
27	CTG Leu 28	Leu a 00 * AAC	GAT Asp 	GAG Glu 21	Glu 36 310 GTG	CAG Gln a	Leu * GTC	Trp 2820 crg	Ala CRF	Glu RF[]	Val 1] 29: GCC	Ser a 30 * CAC	Gla a	Ala 2 CCC	Gly a 840 CAG	Thr a	Val a;	Leu 2950 GCC	Asp>
27	CTG Leu 28	Leu a 00 * AAC	GAT Asp 2 CAC His	GAG Glu 21 ACG Thr	Glu 310 * GTG Val	CAG Gln a	Leu * GTC Val	Trp 2820 crg Leu	Ala CRF GCC Ala	RF[: * AGC Ser	Val 23: GCC Ala	Ser a 30 * CAC His	Gla a ccc Arg	Ala 2 CCC Pro	Gly a 840 CAG Gln	Thr a GGC Gly	Val a; CCG Pro	Leu 2850 * GCC Ala	Asp>
27	CTG Leu 28	Leu a 00 * AAC Ass	GAT Asp CAC His	GAG Glu 21 ACG Thr	Glu a BlO * GTG Val	CAG Gln a GGC Gly	Leu * GTC Val	Trp a2820 crg Leu	Ala CRF GCC Ala ORF	RF[: * AGC Ser	Val 23: GCC Ala	Ser a 30 * CAC His	Gln a CGC Arg	Ala 2 CCC Pro	Gly a 840 CAG Gln a	GGC Gly	Val a;	GCC Ala	Aab>
27	CTG Leu 28	Leu a 00 * AAC	GAT Asp CAC His	GAG Glu 21 ACG Thr	Glu a BlO * GTG Val	CAG Gln a	Leu * GTC Val	Trp a2820 crg Leu	Ala CRF GCC Ala	RF[: * AGC Ser	Val 23: GCC Ala	Ser a 30 * CAC His	Gln a CGC Arg	Ala 2 CCC Pro	Gly a 840 CAG Gln a	Thr a GGC Gly	Val a; CCG Pro	GCC Ala	Asp>
27	CTG Leu 28 AGC Ser	Leu a 00 * AAC ASI a 28	GAT Asp CAC His a60	GAG Glu ACG Thr	Glu a GTG Val a GCG GCG	GGC Gly a STO	t GTC Val	Trp 2820 * CTG Leu * ATC	GCC Ala ORF 2880	# AGC Ser RF[]	Val 29: GCC Ala 1) _	Ser a 30 * CAC His a 28	Gla a CGC Arg a 90	Ala 2 CCC Pro a	Gly a 840 CAG Gln a 2	GGC Gly a GCC	Val CCG Pro a	Leu 2950 GCC Ala aa	GAC Asp>
27	CTG Leu 28 AGC Ser	Leu a 00 * AAC Ass a 28 TGG	CAC His a	GAG Glu ACG Thr GCC -Ala	Glu a 310 * GTG Val a 27 GCG Ala	CAG GIn a GGC Gly a S70 Yal	* GTC Val	Trp 2820 * CTG Leu ATC	GCC Ala ORF 2880 TAC	# AGC Ser RF[]	Val 29: GCC Ala 1) _ AGC Ser	Ser 30 * CAC His 28 GAC Asp	Gln CGC Arg GAC Asp	Ala 2 CCC Pro a ACC	Gly a CAG Gln a CGC Arg	GGC Gly a GCC Ala	Val CCG Pro a;	GCC Ala CCC Pro	Asp> GAC Asp> L> GAC Asp> L> ASC Asn>
27	CTG Leu 28 AGC Ser	Leu a 00 * AAC Ass a 28 TGG	CAC His a	GAG Glu ACG Thr GCC -Ala	Glu a 310 * GTG Val a 27 GCG Ala	CAG GIn a GGC Gly a S70 Yal	* GTC Val	Trp 2820 * CTG Leu ATC	GCC Ala ORF 2880 TAC	# AGC Ser RF[]	Val 29: GCC Ala 1) _ AGC Ser	Ser 30 * CAC His 28 GAC Asp	Gln CGC Arg GAC Asp	Ala 2 CCC Pro a ACC	Gly a CAG Gln a CGC Arg	GGC Gly a GCC Ala	Val CCG Pro a;	GCC Ala CCC Pro	GAC Asp>
27	CTG Leu 28 AGC Ser	Leu a 00 * AAC Ass a 28 TGG	CAC His a	GAG Glu 2! ACG Thr a GCC -Ala	Glu a 310 * GTG Val a 27 GCG Ala	GGC Gly a GTG Val	* GTC Val	Trp 2820 * CTG Leu ATC Ile	GCC Ala ORF 2880 * TAC Tyr	# AGC Ser RF[]	Val 29: GCC Ala 1) _ AGC Ser	Ser 30 * CAC His 28 GAC Asp	Gln CGC Arg GAC Asp	Ala 2 CCC Pro a ACC Thr	Gly a CAG Gln a CGC Arg	GGC Gly a 900 * GCC Ala	Val CCG Pro a;	GCC Ala CCC Pro	Asp> GAC Asp> L> GAC Asp> L> ASC Asn>
27	AGC Ser	Leu a a 00 AAC Ass a 28 TGG TIP	CAC His a 60 CGC Arg a	GCC Ala	Glu a 310 b GTG Val a GCG Ala a	GGC Gly a GTG Val a 2	* GTC Val a CTG Leu	Trp a 2820 * CTG Leu ATC Ile	GCC Ala ORF 2880 * TAC TYT ORF	GIU RF[] * AGC Ser RF[] GCG Ala RF[Val 1) 23: GCC Ala 1) * AGC Ser 1)	Ser 20 CAC His a 28 GAC Asp	Gla CGC Arg a 90 KASP Asp	Ala 2 CCC Pro a ACC Thr a 50	Gly a CAG Gln a CGC Arg	GGC Gly a GCC Ala a 2	CAC His a 960	GCC Ala CCC Pro	Asp> GAC Asp> 1 > 2910 AAC Asn>
27	CGC	Leu a O AAC ABB TGG TTP AGC	GAT Asp CAC His a CGC Arg a 29	ACG Thr ACG-Alaa GCC GCC GCG GGGGGCC	Glu GTG GTG Val GCG Ala GTG	CAG GIn a GGC Gly a GTG Val a ACC	GTC Val a CTG Leu a CTG	Z820 * CTG Leu ATC Ile	GCC Ala ORF 2880 TAC TYT ORF	GIU RF[] * AGC Ser RF[] GCG Ala RF[Val 23: GCC Ala 1) AGC Ser 1)	Ser 20 CAC His 28 GAC Asp	Gla CGC Arg a 90 GAC Asp a 29	Ala 2 CCC Pro a ACC Thr a 50	Gly a CAG Gln a CGC Arg a	GGC Gly GCC Ala	CCG Pro a CAC His a GGC	GCC Ala CCC Pro	GAC Asp> 1 > 2910 AAC Asn> 1
27	CGC Ars	Leu a OO AAC ABB Z8 TGG TTP a AGC Ser	CAC His a CGC Arg a CTC Val	GCC Ala	GIU A GTG Val GCG Ala GTG Val	CAG GIn GGC GGLy GTG Val ACC Thr	GTC Val a CTG Leu a CTG Leu Leu Leu	Z820 CTG Leu ATC Ile CGG Arg	GCC Ala ORF 2880 TAC TYT ORF	AGC Ser RF() GCG Ala RF() 2940 * CGC Arg	Val 28: GCC Ala 1] AGC Ser 1] GGG Gly	Seral	Gla CGC Arg a 90 GAC Asp 29 29	Ala 2 CCC Pro a ACC Thr a 50 * CCC	Gly a CAG Gln a CGC Arg a GGC Gly	GGC GLY GCC Ala	CCG Pro a CAC His a GGC	CTG Leu	Asp> GAC Asp> 1 > 2910 AAC Asn>
27	CGC Arg	Lett a OO AAC ASI 28 TGG TIP AGC Ser	CAC His a CGC Arg a CTC Val	GAG Glu 20 ACG Thr GCC -Ala - GCG Ala GCG Ala	Glu GTG GTG GTG GCG Ala GTG GCG Ala GTG GCG Ala GTG GTG Ala	CAG GIn GGC GGLy GTG Val ACC Thr	CTG Leu	Trp Trp Trp Trp Trp Trp CTG Leu ATC Ile ATC ATC Arg Arg	GCC Ala ORF 2880 TAC TYT ORF	Glu RF[: * AGC Ser RF[: GCG Ala RF[2940 * CGC Arg RF[Vall	Seral	Gla CGC Arg a 90 GAC Asp 29 29	Alaa 2 CCCC Pro a ACC Thr a CCCC Pro a CCCC Pro a ACCC Thr a ACCC Pro a ACCC	Gly CAG Gln a 2 CGC Arg a 4 GGC Gly a	GGC GLY GCC Ala	CAC His a GGC GGC GIY	GCC Ala CCC Pro CTG Leu Leu CTG Leu	Asp> GAC Asp> 1
27	CGC Arg	Leu AAC TGG TTP AGC Ser	CAC His a CGC Arg a CTC Val	GGG Glu 20 ACG Thr GCC Ala GCG Ala 29	Glu GTG Val GCG Ala GTG GTG Val * GTG GTG Val * GTG Val * GTG Val	CAG GIn GGC Gly 870 * GTG Val a ACC Thr a	CTG	Trp a CTG Leu ATC Ile ATC ATS CGG Ars	Ala CRF GCC Ala ORF 2880 * TAC TYC ORF CTG Leu	Glu * AGC Ser RF[GCG Ala RF [CGC Arg RF [*	Val 1	Seral	Gla a CGC Arg a GAC Asp a CCC Arg a	Alaa 2 CCCC Pro ACC Thr CCCC Pro a 30	Gly CAG Gln CAG Gln Arg GGC Gly a 10	GGCC Gly a GCC Alaa CCCG Pro a	Val CCG Pro CAC His a GGC Gly 3	Leu 2950 * GCC Ala 2 2 4 CCC Pro a 2 4 CTG Leu 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2	Asp> GAC Asp> Asp> AAC Asn> CTC Val>
27	CGC Ala CGC Arg	Letu a	GAT ASP CAC CAC Arg a 29 GTC Val a ACG	ACG Thr a GCC Ala a GCG Ala a GCG GCG Ala a GCG GCG Ala a GCG GCG Ala a GCG Ala a GCGC Ala a A GCGC Ala a A GCGC Ala a GCGC Ala a A GCGC A A A A A A A A A A A A A A A A	Glu * GTG Val * GCG Ala * GTG Val * TAC	CAG GIN GGC Gly 870 * GTG Val ACC Thr	Leu * GTC Val a CTG Leu a CTG Leu a CTG GAC	Trp a 2820 * CTG Leu a ATC Ile a CGG Arg a AAC	Ala CRF GCC Ala ORF TAC TYT ORF CTG Leu ORF	# AGC Ser RF[GCG Ala RF[CGC Arg RF[* CGC Arg RF[* CTC	Val 1	Seral	Gla a CGC Arg a GAC Asp a 29 ccc Pro a	Alaa 2 CCCC Pro ACC Thr ACC Pro a 30 CCC GACC GACC GACC	Gly cage cage cage cage cage cage cage cage	GGC Gly 900 CCC Ala a C CCG Pro a C GAG	Val CCG Pro CAC His a GGC Gly TGG	Leu 2850 x GCC Ala 2 2 5 CCC Pro a 2 5 CTG Leu 2 2 CTG	GAC Asp> 1 > 2910 AAC Asn> CGTC Val>
27	CGC Ala CGC Arg	Letu a	GAT ASP CAC CAC Arg a ACG Thr	GCC Ala GCG Ala GCG Ala GCG Ala ACG Ala GCG Ala Ala ACG Ala ACG Ala ACG ACG ACG ACG ACG ACG ACG ACG ACG AC	Glu * GTG Val * GCG Ala * GTG Val * TAC Tyr	CTG Leu	CTG Leu a CTG Leu a CTG Leu A GAC Asp	Trp 2820 CTG Leu ATC Ile ATC Arg Arg AAC Asn	Ala CRF GCC Ala ORF TAC TYT ORF CTG Leu ORF	# AGC Ser RF[CGC Ala RF[2940 * CGC Arg RF[* CTC Leu	Val	Seral	Gla a CGC Arg a GAC Asp a Z9 CCC Pro a CCC Pro	Alaa 2 2 CCC Pro a ACC Thr a CCC Pro a 30 GAC Asp	Gly CAG Gln CGC Arg GGC Gly GGC GGL GGC GGL GGC GGC GGC GGC GGC	GGC Gly a GCC Ala a C CCG Pro	Val CCG Pro CAC His a GGC Gly TGG Trp	Leu Sesso GCC Ala Ala CCCC Ala Arg	GAC Asp> 1 910 AAC Asn> GTC Val> CGC Arg>
27	CGC Ala CGC Arg	Letu a	GAT ASP CAC CAC Arg a ACG Thr	GCC Ala GCG Ala GCG Ala GCG Ala ACG Ala GCG Ala Ala ACG Ala ACG Ala ACG ACG ACG ACG ACG ACG ACG ACG ACG AC	Glu * GTG Val * GCG Ala * GTG Val * TAC Tyr	CTG Leu	CTG Leu a CTG Leu a CTG Leu A GAC Asp	Trp a 2820 * CTG Leu a ATC Ile a CGG Arg a AAC	Ala CRF GCC Ala ORF TAC TYT ORF CTG Leu ORF	# AGC Ser RF[CGC Ala RF[2940 * CGC Arg RF[* CTC Leu	Val	Seral	Gla a CGC Arg a GAC Asp a Z9 CCC Pro a CCC Pro	Alaa 2 2 CCC Pro a ACC Thr a CCC Pro a 30 GAC Asp	Gly CAG Gln CGC Arg GGC Gly GGC GGL GGC GGL GGC GGC GGC GGC GGC	GGC Gly a GCC Ala a C CCG Pro	Val CCG Pro CAC His a GGC Gly TGG	Leu Sesso CCC Pro CTG Leu CCG Arg Arg	GAC Asp> 1 910 AAC Asn> GTC Val> CGC Arg>

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CTG GGC CGG CCC GTC TTC CCC ACG GCA GAG CAG TTC CGG CGC ATG CGC GCG GCT GAG
 Leu Gly Arg Pro Val Phe Pro Thr Ala Glu Gln Phe Arg Arg Met Arg Ala Ala Glu>
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 Asp Pro Val Ala Ala Ala Pro Arg Pro Leu Pro Ala Gly Gly Arg Leu Thr Leu Arg>
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 CCC GCG CTG CGG CTG CCG TCG CTT TTG CTG GTG CAC GTG TGT GCG CGC CCC GAG AAG
 Pro Ala Leu Arg Leu Pro Ser Leu Leu Leu Val His Val Cys Ala Arg Pro Glu Lvs>
 a a a a a a ORF RF[1] a a a a a a a a
 CCG CCC GGG CAG GTC ACG CGG CTC CGC GCC CTG CCC CTG ACC CAA GGG CAG CTG GTT
 Pro Pro Gly Gln Val Thr Arg Leu Arg Ala Leu Pro Leu Thr Gln Gly Gln Leu Val>
 a a a a a a ORF RF[1] a a a a a a a a a
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 CTG GTC TGG TCG GAT GAA CAC GTG GGC TCC AAG TGC CTG TGG ACA TAC GAG ATC CAG
 Leu Val Trp Ser Asp Glu His Val Gly Ser Lys Cys Leu Trp Thr Tyr Glu Ile Gln>
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 Phe Ser Gln Asp Gly Lys Ala Tyr Thr Pro Val Ser Arg Lys Pro Ser Thr Phe Asp>
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  CTC TTT GTG TTC AGC CCA GAC ACA GGT GCT GTC TCT GGC TCC TAC CGA GTT CGA GCC
 Leu Phe Val Phe Ser Pro Asp Thr Gly Ala Val Ser Gly Ser Tyr Arg Val Arg Ala>
    a a a a a a a ORF RF[1] a a a a a a a a a
      3430
  CTG GAC TAC TGG GCC CGA CCA GGC CCC TTC TCG GAC CCT GTG CCG TAC CTG GAG GTC
  Leu Asp Tyr Trp Ala Arg Pro Gly Pro Phe Ser Asp Pro Val Pro Tyr Leu Glu Val>
      a a a a a ORF RF(1) a a a a a a a a a
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  Pro Val Pro Arg Gly Pro Pro Ser Pro Gly Asa Pro>
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  GTTGCACCTC CACCGGCAGT CAGCGAGCTG GGGCTGCACT GTGCCCATGC TGCCCTCCCA TCACCCCCTT
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AAAAAAAAAA AAAAAAAAG AATTOOTGGA GCCCGGGGGA TCCACTAGTT CTAGAGGGCC CGTTTAAACC 3760 3770 3780 3790 3800 3810 3820 CGCTGATCAG CCTCGACTGT GCCTTCTAGT TGCCAGCCAT CTGTTGTTTG CCCCTCCCC GTGCCTTCCT 3830 3840 3850 3860 3870 3880 3890 TGACCCTGGA AGGTGCCACT CCCACTGTCC TTTCCTAATA AAATGAGGAA ATTGCATCGC ATTGTCTGAG 3900 3910 3920 3930 3940 3950 3960 TAGGTGTCAT TCTATTCTGG GGGGTGGGGT GGGGCAGGAC AGCAAGGGGG AGGATTGGGA AGACAATAGC 3970 3980 3990 4000 4010 4020 4030 AGGCATGCTG GGGATGCGGT GGGCTCTATG GCTTCTGAGG CGGAAAGAAC CAGCTGGGGC TCGAGAGCTT 4040 4050 4060 4070 4080 4090 4100 GGCGTAATCA TGGTCATAGC TGTTTCCTGT GTGAAATTGT TATCCGCTCA CAATTCCACA CAACATACGA GCCGGAAGCA TAAAGTGTAA AGCCTGGGGT GCCTAATGAG TGAGCTAACT CACATTAATT GCGTTGCGCT 4180 4190 4200 4210 4220 4230 4240 CACTGCCCGC TTTCCAGTCG GGAAACCTGT CGTGCCAGCT GCATTAATGA ATCGGCCAAC GCGCGGGGAG 4250 4260 4270 4280 4290 4300 4310 AGGCGGTTTG CGTATTGGGC GCTCTTCCGC TTCCTCGCTC ACTGACTCGC TGCGCTCGGT CGTTCGGCTG 4320 4330 4340 4350 4360 4370 4380 CGGCGAGCGG TATCAGCTCA CTCAAAGGCG GTAATACGGT TATCCACAGA ATCAGGGGAT AACGCAGGAA 4390 4400 4410 4420 4430 4440 4450 AGAACATGTG AGCAAAAGGC CAGCAAAAGG CCAGGAACCG TAAAAAGGCC GCGTTGCTGG CGTTTTTCCA 4460 4470 4480 4490 4500 4510 4520 TAGGCTCCGC CCCCCTGACG AGCATCACAA AAATCGACGC TCAAGTCAGA GGTGGCGAAA CCCGACAGGA 4530 4540 4550 4560 4570 4580 4590 CTATAÁAGAT ACCAGGCGTT TCCCCCTGGA AGCTCCCTCG TGCGCTCTCC TGTTCCGACC CTGCCGCTTA 4600 4610 4620 4630 4640 4650 4660 CCGGATACCT GTCCGCCTTT CTCCCTTCGG GAAGCGTGGC GCTTTCTCAA TGCTCACGCT GTAGGTATCT CAGTTCGGTG TAGGTCGTTC GCTCCAAGCT GGGCTGTGTG CACGAACCCC CCGTTCAGCC CGACCGCTGC 4740 4750 4760 4770 4780 4790 4800 GCCTTATCCG GTAACTATCG TCTTGAGTCC AACCCGGTAA GACACGACTT ATCGCCACTG GCAGCAGCCA

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4810 4820 4830 4840 4850 4860 4870 CTGGTAACAG GATTAGCAGA GCGAGGTATG TAGGCGGTGC TACAGAGTTC TTGAAGTGGT GGCCTAACTA 4880 4890 4900 4910 4920 4930 4940 CGGCTACACT AGAAGGACAG TATTTGGTAT CTGCGCTCTG CTGAAGCCAG TTACCTTCGG AAAAAGAGTT 4950 4960 4970 4980 4990 5000 GGTAGCTCTT GATCCGGCAA ACAAACCACC GCTGGTAGCG GTGGTTTTTT TGTTTGCAAG CAGCAGATTA 5020 5030 5040 5050 5060 5070 CGCGCAGAAA AAAAGGATCT CAAGAAGATC CTTTGATCTT TTCTACGGGG TCTGACGCTC AGTGGAACGA ARACTCACGT TAAGGGATTT TGGTCATGAG ATTATCAAAA AGGATCTTCA CCTAGATCCT TTTAAATTAA 5160 5170 5180 5190 5200 5210 5220 • • • • • • • • • • • • • • • • • • AAATGAAGTT TTAAATCAAT CTAAAGTATA TATGAGTAAA CTTGGTCTGA CAGTTACCAA TGCTTAATCA 5230 5240 5250 5260 5270 5280 5290 GTGAGGCACC TATCTCAGCG ATCTGTCTAT TTCGTTCATC CATAGTTGCC TGACTCCCCG TCGTGTAGAT 5300 5310 5320 5330 5340 5350 5360 AACTACGATA CGGGAGGGCT TACCATCTGG CCCCAGTGCT GCAATGATAC CGCGAGACCC ACGCTCACCG GCTCCAGATT TATCAGCAAT AAACCAGCCA GCCGGAAGGG CCGAGCGCAG AAGTGGTCCT GCAACTTTAT CCGCCTCCAT CCAGTCTATT AATTGTTGCC GGGAAGCTAG AGTAAGTAGT TCGCCAGTTA ATAGTTTGCG CAACGITGIT GCCATTGCTA CAGGCATCGI GGTGTCACGC TCGTCGTTTG GTATGGCTTC ATTCAGCTCC 5580 5590 5600 5610 5620 5630 5640 GGTTCCCAAC GATCAAGGCG AGTTACATGA TCCCCCATGT TGTGCAAAAA AGCGGTTAGC TCCTTCGGTC CTCCGATCGT TGTCAGAAGT AAGTTGGCCG CAGTGTTATC ACTCATGGTT ATGGCAGCAC TGCATAATTC 5720 5730 5740 5750 5760 5770 5780 TCTTACTGTC ATGCCATCCG TAAGATGCTT TTCTGTGACT GGTGAGTACT CAACCAAGTC ATTCTGAGAA 5790 5800 5810 5820 5830 5840 5850 TAGTGTATGC GGCGACCGAG TTGCTCTTGC CCGGCGTCAA TACGGGATAA TACCGCGCCA CATAGCAGAA \$860 \$870 \$880 \$890 \$900 \$910 \$920
 CTTTAAAAAGT
 GCTCATCATT
 GGAAAACGTT
 CTTCGGGGCG
 AAAACTCTCA
 AGGATCTTAC
 CGCTGTTGAG

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 5950
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 ATGTAACCCA
 CTCGTGCACC
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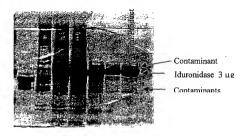
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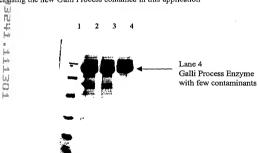
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 GAAAAGGCC
 ACCTGACGTC

Gel using the Kakkis et al 1994, published procedure for purification



Gelusing the new Galli Process contained in this application

0



- 1. Molecular Weight Marker
- 2. Prior Process Carson (nonpublished) Batch 2000C9001 Reference Reduced (7.5 μg)
- 3. Same Batch 2000C9001 Reference Reduced (5.0 µg)
- 4. Galli Process Enzyme Batch P10006 (5.0 μg)

FIGURE 3A IDURONIDASE PRODUCTION USING THE GALLI PROCESS

Iduronidase Enzyme Activity During Production

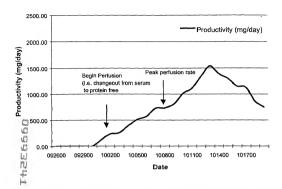
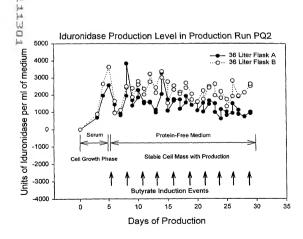


Figure 3B. Iduronidase Production Using Butyrate Induction



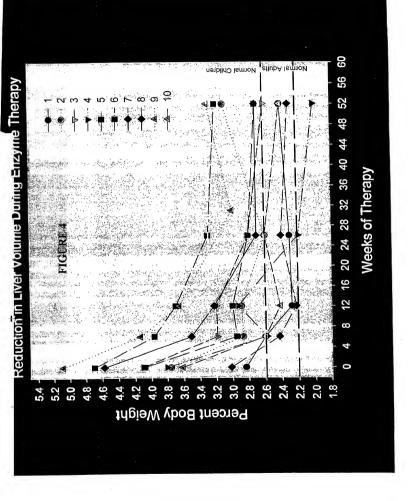
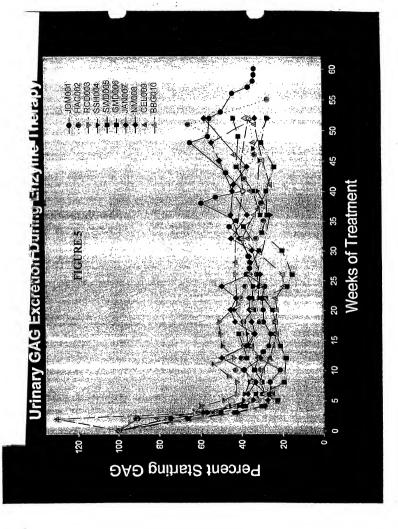
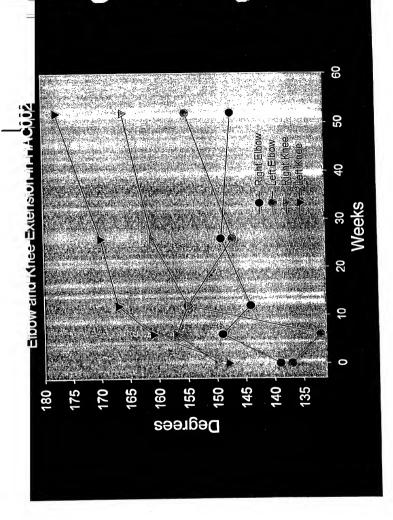


FIGURE 4





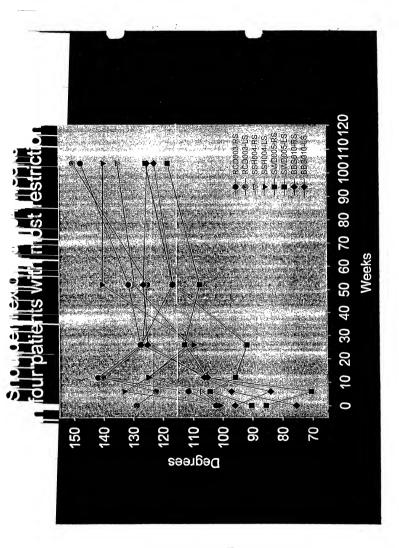


FIGURE 7

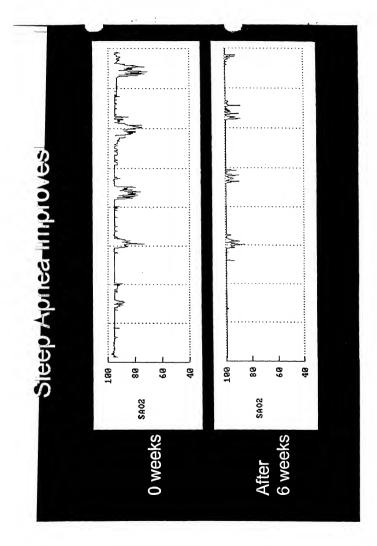
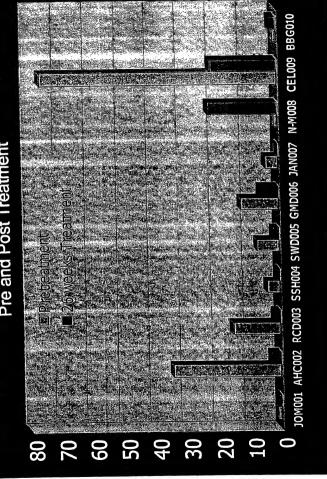
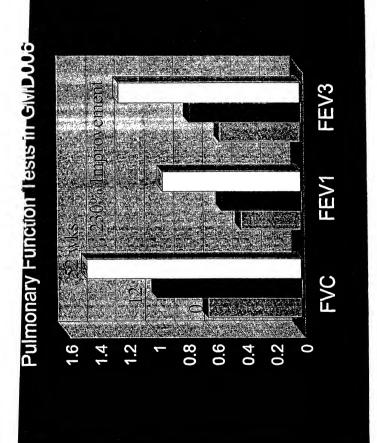


FIGURE 8

Apneas + Hypopheas During Sleep Pre and Post Treatment





Increased Height Growth Velocity

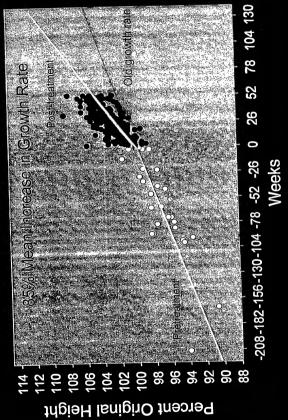


FIGURE 12.

COMPARISON OF HOST PROTEIN CONTAMINATION BETWEEN A PRIOR AND THE NEW GALLI PROCESS

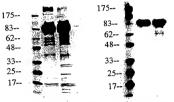
Chinese Hamster Ovary Host Protein Contamination by ELISA Assay

Source and Batch Number	CHOP PROTEIN CONTAMINATION (microgram per milligram)	PERCENT CHOP CONTAMINATION	PURITY OF THE ENZYME FROM CHOP
Prior Process (Carson/REI)			
C9002	14	1.4%	98.6%
C9003	24	2.4%	97.6%
C9004	16	1.6%	98.4%
New Process (Galli)			
P1003	<1.3	<0.13%	>99.9%
P1006	1.2	0.12%	99.9%
P1007	< 0.6	<0.06%	>99.9%
P1008	< 0.67	<0.067%	>99.9%

Comparison of Galli and Carson Material

1 2 3

1 2 3



anit-IDU Western blot SDS-PAGE silver stain 1:50,000

- 1 Marker
- 2 Galli Referenced-0201
- 3 Carson C9002

5ug/lane